The peripheral dopaminergic system: morphological analysis, functional and clinical applications*

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SUMMARY

In vivo administration or *in vitro* application of dopamine or of dopamine receptor agonists induce vasodilatation in the cerebral, coronary, renal and mesenteric vascular beds and cause hypotension. Moreover, dopamine stimulates cardiac contractility and induces diuresis and natriuresis. Peripheral (cardiovascular and renal) dopamine receptors belong to the D1-like and D2-like receptor superfamilies, thought to be located post-junctionally and pre-junctionally respectively. Stimulation of vascular D1-like receptors causes direct vasodilatation and reduction of vascular resistance. Stimulation of vascular D2-like receptors causes indirect vasodilatation, resulting from inhibition of sympathetic vasoconstrictor tone. Combined radioligand binding assay and light microscope autoradiography have investigated the anatomical localization of cardiovascular and renal dopamine D1-like and D2-like receptors in different animal species including humans. The application of molecular biology techniques to dopamine receptor research has shown that the picture of dopamine receptor subtypes is more complicated than it was suggested in the past, with at least 5 subtypes belonging to the dopamine D1-like (D1 and D5 receptors) and D2-like (D2, D3 and D4 receptors) superfamilies. The development of antibodies raised against selected sequences of dopamine receptor subtypes has allowed a more detailed characterization of the density and pattern of peripheral dopamine receptors. Dopamine receptor protein immunohistochemistry confirmed the localization of dopamine D1 and D5 receptors in the tunica media of systemic arteries and of prejunctional dopamine D2-D4 receptors closely associated with sympathetic neuroeffector junctions. The distribution and the density of prejunctional dopamine D2-like receptors was different in various vascular beds investigated. The kidney expresses the 5 different subtypes of dopamine receptors, displaying a not homogeneous vascular and tubular localization.. Dopamine acting as autocrine or paracrine substance is probably involved in the regulation of immune activity. Human peripheral blood lymphocytes contain dopamine and express plasma membrane and vesicular dopamine transporters

as well as dopamine D3, D4 and D5 receptors. Another recently characterized peripheral dopaminergic system is located in the lung. Dopamine D1-like receptor immunoreactive structures were found in a small percentage of nerve fibres contained in pulmonary nerve trunks. D1-immunoreactive nerve fibres were approximately 2-3% of total fibres, whereas D5-immunoreactive fibres accounted approximately for 5-6% of total fibres. Also dopamine D2-like receptor immunoreactive fibres were found in pulmonary trunks. D2-immunoreactive fibres accounted for approximately 3-5% of total nerve fibres, D3 receptor-immnunoreactive fibres accounted for about 8-10% of total nerve fibres, whereas only rare profiles of D4 receptor protein-immunoreactive fibres were observed. Dopamine recepetor protein immunostaining was also found in neurons of nodose ganglion, that display immunoreactivity for different neuropeptides. Based on the correspondence between the number of dopamine receptor immunoreactive pulmonary nerve fibres and of vagal ganglionic neurons immunoreactive for dopamine receptors it is possible to hypothesize that these receptors are located on pulmonary afferents. In spite of the heterogeneity of peripheral systems expressing dopamine receptors, analysis of their localization with appropriate microanatomical techniques may contribute to investigate their role in health and disease.